Claims

1 A compound comprising an amino acid sequence having at the most 12 amino acid residues from the amino acid sequence of neural cell adhesion molecule (NCAM), or a mimic thereof comprising an amino acid sequence having at the most 12 amino acid residues, said compound comprising

the sequence $(K/R)_{0-1}$-K/R-X-K/R), wherein X is any amino acid, and/or

the sequence (K/R)-X-X-X-(K/R)-X-(E/D)-(L/I/V/F)-X-(L/I/V/F), wherein X is any amino acid residue, and/or

the sequence selected from the group (E/D)-X-(K/R)-(L/I/V/F)-X-(L/I/V/F), (E/D)-X-(K/R)-(L/I/V/F)-(L/I/V/F), (E/D)-X-X-X-X-(E/D)-X-(K/R)-(L/I/V/F), (E/D)-X-X-X-(E/D)-X-(K/R)-(L/I/V/F) or (E/D)-X-X-(E/D)-X-(K/R)-(L/I/V/F),

said compound being capable of binding to the NCAM Ig1-Ig2 domains and of stimulating or promoting neurite outgrowth from NCAM presenting cells and/or proliferation hereof.

2 The compound according to claim 1, capable of binding to the NCAM Ig1 domain.

3 The compound according to the claims 1 or 2, capable of binding to the homophilic binding site of the Ig1-Ig2 domains which is constituted by the Ig1 domain.

4 The compound according to any of the claims 1, 2 or 3, wherein said compound is a fragment of the NCAM Ig2 polypeptide.

5 The compound of claim 4, capable of binding to the NCAM Ig1 domain through a binding motif which comprises at least 2 basic amino acid residues.

6 The compound of claim 5 comprising at least 2 basic amino acid residues within a sequence of 10 amino acid residues.

7 The compound of claim 6, comprising at least 2 basic amino acid residues within a sequence of 3 amino acid residues.

8 The compound according to the claims 8-12, comprising the sequence K/R-K/R-X-K/R or K/R-X-K/R, wherein X is any amino acid, more suitably the sequence K/R-P-K/R, K/R-K/R-P-K/R, K/R-K/R-E-K/R or K/R-K/R-E-K/R, even more suitably the sequence K-P-K, K-K-P-K, K-K-E-K or K-K-E-R and most suitably the sequence A-S-K-K-P-K-R-N-I-K-A (SEQ ID NO:1), A-K-K-E-R-Q-R-K-D-T-Q (SEQ ID NO:2), or A-R-A-L-N-W-G-A-K-P-K (SEQ ID NO:3).

9 The compound according to claim 1, having the sequence A-S-K-K-P-K-R-N-I-K-A (SEQ ID NO:1), A-K-K-E-R-Q-R-K-D-T-Q (SEQ ID NO:2), or A-R-A-L-N-W-G-A-K-P-K (SEQ ID NO:3).

10 The compound according to any of claims 5-9, wherein one or more of the amino acid residues is modified, such as being acetylated.

11 The compound according to any of the claims 5-10, being identical to a part of the NCAM Ig2 domain.

12 The compound according to any of the claims 5-10, being a fragment of the NCAM Ig2 domain.

13 The compound according to any of claims 5-12, capable of binding to the NCAM Ig2 binding site on the NCAM Ig1 domain.

14 The compound according to any of claims 5-12, capable of binding to a binding site on the NCAM Ig1 domain, wherein the binding site is different from the NCAM Ig2 binding site.

15 The compound according to claim 14, wherein the number of amino acid residues in the sequence of the binding motif is within 12 amino acid residues.

16 The compound according to any of the claims 14 and 15, wherein the number

of amino acid residues in the sequence of the binding motif is within 8 amino acid residues.

17 The compound according to the claims 12-16, wherein the peptide comprises the sequence (K/R)-X-(E/D)-(L/I/V/F)-X-(L/I/V/F), (K/R)-X-X-X-(K/R)-X-(E/D), (K/R)-X-X-(K/R)-X-(E/D) or (K/R)-X-(L/I/V/F)-X-(L/I/V/F), wherein X is any amino acid residue ,more suitably the sequences (K/R)-X-X-X-(K/R)-X-(E/D)-(L/I/V/F), (K/R)-X-X-(K/R)-X-(E/D)-(L/I/V/F) or (K/R)-X-X-X-(K/R)-X-(L/I/V/F), even more suitably the sequences (K/R)-X-X-(K/R)-X-(E/D)-(L/I/V/F)-X-(L/I/V/F), (K/R)-X-X-X-(K/R)-X-(L/I/V/F)-X-(L/I/V/F) or (K/R)-X-X-X-(K/R)-X-(E/D)-(L/I/V/F)-(L/I/V/F) and most suitably the sequence GRILARGEINFK (SEQ ID NO: 23).

18 The compound according to claim 17, having the sequence GRILARGEINFK (SEQ ID NO:23).

19 The compound according to any of the claims 12-18, wherein one or more of the amino acid residues is modified, such as being acetylated.

20 The compound according to any of the claims 12-19, being a fragment of, or is identical to a part of the homophilic binding site of the NCAM Ig1-Ig2 domain which is constituted by the Ig2 domain.

21 The compound according to claim 1, capable of binding to the NCAM Ig2 domain.

22 The compound according to the claims 1 or 32, capable of binding to the homophilic binding site of the Ig1-Ig2 domains which is constituted by the Ig2 domain.

23 The compound according to any of the claims 1, 32 or 33, wherein said compound is a fragment of the NCAM Ig1 polypeptide.

24 The compound according to any of the claims 21 and 23 being a peptide, wherein the binding motif comprises at least 2 acidic amino acid residues and at least 1 apolar amino acid.

25 The compound according to claim 24, wherein the number of amino acid residues in the sequence of the binding motif is within 12 amino acid residues.

26 The compound according to claim 27, wherein the number of amino acid residues in the sequence of the binding motif is within 9 amino acid residues.

27 The compound according to the claims 21-26, wherein the peptide comprises the sequence (E/D)-X-X-X-(E/D)-X-(K/R)-(L/I/V/F)-X-(L/I/V/F), wherein X is any amino acid residue, more suitably E/D)-X-X-(E/D)-X-(K/R)-(L/I/V/F)-X-(L/I/V/F/) or (E/D)-X-X-(E/D)-X-(K/R)-(L/I/V/F)-(L/I/V/F), even more suitably the sequences (E/D)-X-X-X-X-(E/D)-X-(K/R)-(L/I/V/F)-(L/I/V/F), (E/D-X-X-X-(E/D)-X-(K/R)-(L/I/V/F)-X-(L/I/V/F) or (E/D)-X-X-X-(E/D)-X-(K/R)-(L/I/V/F)-(L/I/V/F), and most suitably the sequence GEJSVGESKFFL (SEQ ID NO: 26).

28 The compound according to claim 27, wherein the peptide has the sequence GEJSVGESKFFL (SEQ ID NO: 26).

29 The compound according to any of the claims 22-28, wherein one or more of the amino acid residues is modified, such as being acetylated.

30 The compound according to any of the claims 23-29, being a part of the homophilic binding site of the NCAM Ig1-Ig2 domains which is constituted by the Ig1 domain.

31 The compound according to any of the claims 1-30, wherein a fragment thereof is for the use as a medicament.

32 The compound according to claim 31, wherein a fragment thereof is for the manufacture of a medicament for treatment of normal, degenerated or damaged NCAM presenting cells.

33 Use of a compound comprising at the most 12 amino acid residues from the amino acid sequence of neural cell adhesion molecule (NCAM), or a fragment thereof, or a mimic thereof as defined in any of claims 1-32, capable of binding

to the NCAM Ig1-Ig2 domains and of stimulating or promoting neurite outgrowth from NCAM presenting cells and/or proliferation hereof.

34 The use according to claim 33, wherein said compound are for the use as a medicament.

35 The use according to claim 34, wherein said compound are for the manufacture of a medicament for treatment of normal, degenerated or damaged NCAM presenting cells.

36 The use according to claim 34, for the manufacture of a medicament for treatment comprising the stimulation of outgrowth from and/or proliferation of N-CAM presenting cells.

37 The use according to claim 34, for the manufacture of a medicament comprising treatment of diseases and conditions of the central and peripheral nervous system, of the muscles or of various organs.

38 The use according to claim 34, comprising treatment of postoperative nerve damage, traumatic nerve damage, impaired myelination of nerve fibers, postischaemic, e.g. resulting from a stroke, Parkinsons disease, Alzheimers disease, dementias such as multiinfarct dementia, sclerosis, nerve degeneration associated with diabetes mellitus, disorders affecting the circadian clock or neuro-muscular transmission, and schizophrenia.

39 The use according to claim 34, comprising treatment of diseases of muscles, including conditions with impaired function of neuro-muscular connections such as genetic or traumatic atrophic muscle disorders.

40 The use according to claim 34, comprising treatment of diseases of various organs, such as degenerative conditions of the gonads, of the pancreas such as diabetes mellitus type I and II, of the kidney such as nephrosis and of the heart, liver and bowel.

41 The use according to claim 34, comprising stimulation of the ability to learn

and/or of the memory.

42 A pharmaceutical composition, comprising one or more of the compounds according to any of the claims 1-32.

43 The pharmaceutical composition according to claim 42, wherein the compound is a fragment of the NCAM Ig1 peptide.

44 The pharmaceutical composition according to claim 42, wherein the compound is a fragment of the NCAM Ig2 peptide.

45 The pharmaceutical composition according to any of the claims 42-44, wherein the compounds are formulated as multimers.

46 The pharmaceutical composition according to any of the claims 42-44, characterised in that the compounds are formulated as dendrimers, such as four peptides linked to a lysine backbone, or coupled to a protein carrier such as BSA.

47 The pharmaceutical composition according to any of the claims 42-46 formulated for oral, percutaneous, intramuscular, intracranial, intraventricular, intranasal or pulmonal administration.

48 The pharmacetical composition according to any of the claims 42-47, characterised in that the pharmaceutical composition comprises an effective amount of one or more of the compounds according to any of the claims 1-32, or a pharmaceutical composition according to any of the claims 42-47 and one or more pharmaceutically acceptable additives or carriers.

49 The pharmacetical composition according to the claims 42-47 for use in the stimulation of learning and/or memory in a subject, characterised in that the composition comprises an effective amount of one or more of the compounds according to any of the claims 1-32 or a pharmaceutical composition according to any of the claims 42-47 and one or more pharmaceutically acceptable additives or carriers.

50 The pharmaceutical composition according to claim 49 formulated for oral, percutaneous, intramuscular, intracranial, intraventricular, intranasal or pulmonal administration.

51 Use of a pharmaceutical composition as defined in claim 50, wherein the composition is in combination with a prosthetic device.

52 The use according to claim 51, wherein the device is a prosthetic nerve guide.

53 A prosthetic nerve guide, characterised in that it comprises one or more of the compounds according to any of the claims 1-32, or a pharmaceutical composition according to any of the claims 42-47.

54 Use according to claim 34, wherein said compound is an NCAM Ig1 fragment for treatment of diseases or conditions of the central and peripheral nervous system, such as postoperative nerve damage, traumatic nerve damage, impaired myelination of nerve fibers, postischaemic, e.g. resulting from a stroke, Parkinsons disease, Alzheimers disease, dementias such as multiinfarct dementia, sclerosis, nerve degeneration associated with diabetes mellitus, disorders affecting the circadian clock or neuro-muscular transmission, and schizophrenia; for treatment of diseases or conditions of the muscles including conditions with impaired function of neuromuscular connections, such as genetic or traumatic atrophic muscle disorders; or for treatment of diseases or conditions of various organs, such as degenerative conditions of the gonads, of the pancreas such as diabetes mellitus type I and II, of the kidney such as nephrosis and of the heart, liver and bowel.

55 Use according to claim 34, wherein said compound is an NCAM Ig2 fragment for treatment of diseases or conditions of the central and peripheral nervous system, such as postoperative nerve damage, traumatic nerve damage, impaired myelination of nerve fibers, postischaemic, e.g. resulting from a stroke, Parkinsons disease, Alzheimers disease, dementias such as multiinfarct dementia, sclerosis, nerve degeneration associated with diabetes mellitus, disorders affecting the circadian clock or neuro-muscular transmission, and schizo-

phrenia; for treatment of diseases or conditions of the muscles including conditions with impaired function of neuro-muscular connections, such as genetic or traumatic atrophic muscle disorders; or for treatment of diseases or conditions of various organs, such as degenerative conditions of the gonads, of the pancreas such as diabetes mellitus type I and II, of the kidney such as nephrosis and of the heart, liver and bowel.